Clinical and Experimental Allergy, 1993. Volume 23, pages 982–985

Histamine-free diet: treatment of choice for histamine-induced food intolerance and supporting treatment for chronical headaches

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Summary

Histamine-induced food intolerance is not IgE-mediated. Skin-prick testing and specific IgE to food allergens are typically negative. Food rich in histamine or red wine may cause allergy-like symptoms such as sneezing, flush, skin itching, diarrhoea and even shortness of breath. The suspected reason is a diminished histamine degradation based on a deficiency of diamine oxidase. As diamine oxidase cannot be supplemented, a histamine-free diet was implemented to reduce histamine intake. Forty-five patients with a history of suffering from intolerance to food or wine ($n=17$) and chronic headache ($n=28$) were put on the diet over months to years. Fish, cheese, hard cured sausages, pickled cabbage and alcoholic beverages had to be avoided. Complaint intensity and drug-use per week prior to and 4 weeks after a histamine-free diet were compared. After 4 weeks on the diet 33/45 patients improved considerably ($P<0{\cdot}01$), eight of them had total remission. In 12/45 patients, however, no changes in symptoms were observed. Symptoms of food or wine intolerance significantly decreased ($P<0{\cdot}02$; treatment of choice), headaches decreased in frequency ($P<0{\cdot}001$), duration and intensity. After eating histamine-rich food symptoms were reproducible and could be eliminated by anti-histamines in most patients. These data indicate the role of histamine in food and wine intolerance and that histamine-rich food causes a worsening of symptoms in patients suffering from chronic headaches. Results obtained support the hypothesis of a deficiency of diamine oxidase in patients with intolerance to food or wine.

Clinical and Experimental Allergy, Vol. 23, pp. 982–985. Submitted 3 December 1992; revised 16 June 1993; accepted 1 July 1993.

Introduction

So called 'food allergy' despite negative allergy tests is common. As several foods may contain high amounts of histamine [1–5], their ingestion sometimes causes allergy-like symptoms such as sneezing, flush, headache, diarrhoea and even shortness of breath. In these patients an increase in plasma histamine after drinking red wine was observed compared with asymptomatic controls [6–8]. In the same patients red wine intolerance could be eliminated by H1-blocker premedication [7,8], indicating the histamine genesis. In patients with intolerance to food and/or wine we consider a diminished histamine degradation based on a deficiency of diamine oxidase, the main enzyme catabolizing histamine in the gut [9].

As diamine oxidase cannot be substituted, a diet with clearly reduced histamine may pose fewer demands on diamine oxidase. Thus, diamine oxidase's capacity may be indirectly enhanced and histamine could be eliminated more easily.

The aim of the present study was to evaluate the therapeutic efficacy of a histamine-free diet in patients intolerant to food and/or wine as well as in patients suffering from chronic headaches.

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Patients and methods

Forty-five patients, 30 women and 15 men, mean age 37·7 years (range 10–60 yr) with suspected histamine-induced

Table 1. Food listed below must be avoided strictly

Histamine-free diet
Fish
Tunny
Sardine
Anchovy
Mackerel
Cheese
Emmenthal
Harzer cheese
Gouda
Roquefort
Tilsiter
Camembert
Cheddar
Hard cured sausages
Salami
Dried ham
Vegetables
Pickled cabbage
Spinach
Tomatoes (ketchup)
Alcoholic beverages
Red wine
White whine
Sparkling wine
Beer

intolerance to food ($n=17$) and chronic headaches ($n=28$) were given the histamine-free diet for 4 weeks (Table 1). Foods listed in Table 1 had to be strictly avoided. All patients had a history of food intolerance over at least 6 months to several years and served as their own controls. After skin-prick testing with standard and food series (Epipharm, Linz, Austria) they were classified according to their diagnoses.

Patients

Group 1 Seventeen patients with intolerance to food or wine showing symptoms such as flush ($n=10$), itching of the skin ($n=8$), itching as well as mucosal swelling in the mouth ($n=5$) congestion of the nose with sneezing ($n=3$), diarrhoea ($n=4$), or shortness of breath ($n=3$) after ingestion of histamine-rich food. Symptoms occurred at least two times per week between 10 to 30 min and 3 hr after ingestion of food as listed in Table 1. Patients were non-atopics with negative allergy tests to food allergens except two patients allergic to animal dander and two patients allergic to birch pollen (17 patients, 11 women, six men; 40·6 yr mean; total IgE: mean 94 kU/l, range 4–310 kU/l).

Group 2 Twenty-eight patients suffering from chronic headaches with at least one weekly attack (mean $3{\cdot}1 \pm 2{\cdot}0$ attacks per week). Patients were non-atopics except three patients allergic to birch pollens (28 patients, 19 women, nine men; 36·0 yr mean; total IgE: mean 71 kU/l, range 2–598 kU/l).

Assessment of success of treatment

Frequency of symptoms per week and drug use per week (non-steroidal-analgesics on demand in the headache group) the month prior to and 4 weeks after histamine-free diet were compared. Success of treatment was assumed when reduction of symptoms and/or reduction of drug use was evident by more than 50% compared with the months before diet, a total remission was classified as cessation of symptoms.

Dietary errors

A dietary error is defined by symptoms after eating any food listed in Table 1.

Statistical analysis

Statistical analysis was carried out using the sign test.

Results

After 4 weeks of diet a reduction of symptoms and/or drug use was evident in 33/45 patients by more than 50% ($P<0{\cdot}01$), eight of them had total remission. However, no changes in symptoms could be observed in 12/45 patients (Table 2).

In 14/17 patients with intolerance to food and/or wine the incidence of symptoms decreased significantly

Table 2. Results in 45 patients after 4 weeks of diet

	Total remission (n)	Improvement >50% (n)	No change of symptoms (n)
Patients with food and wine intolerance ($n=17$)			
$P<0{\cdot}02$	4	10	3
Patients with chronic headaches ($n=28$)			
$P<0{\cdot}001$	4	15	9

($P<0{\cdot}02$). In 19 patients with chronic headaches the success of treatment was evident by a more than 50% reduction of headaches. The incidence of headaches decreased from $3{\cdot}1 \pm 2{\cdot}3$ attacks per week to $1{\cdot}1 \pm 1{\cdot}0$ attacks per week ($P<0{\cdot}001$). Analgesic medication could be reduced from 50% up to 75% in six patients compared with the month prior diet.

Dietary errors after 12 months of treatment

Six women patients with intolerance to food remain stable but report several dietary errors to pickled cabbage, tuna, cheese, tomatoes, spinach and wine, which were reversible to anti-histamine intake (terfenadine, loratadine). However, 2/17 patients lost their symptoms within 6 months of diet. Patients with headaches ($n=8/9$) remain stable but report several dietary errors to cheese, tomatoes and wine.

Discussion

Histamine-induced food intolerance, characterized by a lack of specific IgE and negative skin-prick testing, is defined by intolerance to red wine and allergy-like symptoms after ingestion of food rich in histamine [6–8]. Symptoms of intolerance to a certain food do not always occur, because amounts of histamine vary extensively [1–5], but symptoms are reproducible as described by case history and evidenced by dietary errors.

In patients suffering from headaches or itching of the skin after drinking red wine, plasma histamine did not decrease to basal level after 30 min as observed in controls, but showed an increase. Symptoms of wine intolerance could be eliminated by H1-blocker premedication [6–8].

In patients with intolerance to histamine we postulate a deficiency of diamine oxidase, because histamine seems to be catabolized insufficiently. Thus, elevated histamine levels in blood remain for a prolonged time causing symptoms such as headache, sneezing, diarrhoea, urticaria and even bronchial asthma [6–8,10].

By inhibiting diamine oxidase in animals oral histamine produced massive symptoms such as bronchospasm correlating with a significant increase in plasma histamine [11,12]. Anti-histamines eliminated these symptoms [11,12].

Even in healthy persons massive amounts of ingested histamine cause symptoms such as severe headache and flush, as known in scombroid intoxication [13]. Symptoms occurring 10–30 min after eating food containing histamine can be reduced by anti-histamines [13,14].

Histamine, a biogenic amine formed by bacteria decarboxylating histidine [4], acts as indicator of freshness and hygenic handling of food [14].

Orally ingested histamine is catabolized by diamine oxidase located in the jejunal mucosa [9]. Putrescine or tyramine, occurring in red wine or cheese, are also catabolized by diamine oxidase, causing competitive inhibition of the enzyme [12]. Alcohol and drugs are also remarkable inhibitors of diamine oxidase. Up to the present 94 drugs are known inhibitors of diamine oxidase, such as dihydralazine, isoniazid, clavulanic acid, promethazine, verapamil, metoclopramide and ambroxol hydrochloride [11,12,15–17]. Patients under long-term medication with these drugs and patients in an intensive care unit should therefore be put on a histamine-free diet [18].

By blocking diamine oxidase enteral histamine uptake is enhanced inducing elevated plasma histamine levels [12], which cause inhibition of *N*-methyltransferase, another important enzyme for histamine degradation [12]. Therefore, a deficiency of diamine oxidase is likely to cause the same pathomechanism.

In women intolerant to food we observed remissions occurring in pregnancy with recurrences some weeks after delivery. As diamine oxidase levels are massively enhanced in pregnancy [19,20], a deficiency of diamine oxidase in these food intolerant patients appears likely.

As shown in six women with severe intolerance to food, symptoms vanished with a histamine-free diet but could be reproduced at any time by dietary errors. In addition symptoms could be eliminated by anti-histamine pre-treatment.

Although there is only indirect evidence for the histamine genesis in our patients and although substances such as sulfite [21] are also reduced by the diet, our main arguments are reproducible dietary errors and the reduction of symptoms by anti-histamine pre-treatment.

For patients with histamine-induced intolerance to food we recommend a histamine-free diet as the therapy of choice. A histamine-free diet may serve as supporting and prophylactic treatment in headache, which has been induced experimentally by histamine infusion [22] and red wine provocation [23]. After 12 months of diet 8/9 patients with headaches remain stable but report dietary errors to cheese, tomatoes and wine.

In addition, we tested histamine-free diet in patients with allergic bronchial asthma, atopic dermatitis and chronic urticaria. Symptoms could be remarkably reduced as shown in one man who lost his shortness of breath completely while on the diet [8]. As intolerance to histamine seems to occur in allergic patients too, a histamine-free diet appears to be beneficial for patients with allergic diseases, especially as diamine oxidase activity seem to be reduced in allergic diseases [24,25].

Although this is an open study based on the hypothesis of a deficiency or reduced activity of diamine oxidase,

according to the obtained data, patients with intolerance to food and/or wine and patients with chronic headaches seem to have increased sensitivity to histamine. Moderate amounts of histamine in food can therefore induce massive symptoms as additionally evidenced by dietary errors and elimination of symptoms by anti-histamines.

Histamine-rich food causes allergy-like symptoms in sensitive patients. As avoidance of histamine rich food is a simple and harmless treatment, alcoholic beverages and food containing histamine, such as cheese should be labelled.

Acknowledgements

We want to thank Dipl. Ing. Dr Udo Pechanek (Forschungsinstitut für Ernährungswirtschaft, Wien) for support with the scientific data and Professor Dr Viktor Scheiber (Institut für medizinische Statistik, Wien) for statistical analysis.

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